Poly[(R)-3-hydroxyalkanoates] – The Fourth Family of Biopolymers: Contributions of an Organic Chemist

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Originally, we considered PHB as a source of (R)-3-hydroxybutanoic acid (HB), a chiral synthetic building block [1], the enantiomer of the yeast reduction product of 3-oxo-butanote [2]. We learned how to modify the structure of this simple molecule at each and every position of the C₆ skeleton [3–5] and to apply the principles developed with it to other 3-hydroxy-alkanoates (PHA) as well as to 3-amino-carboxylic acids [6,7].

Over the years, we became more and more interested in biological, biochemical, medicinal, and material science aspects of PHB and the other poly(hydroxyalkanoates) (PHAs). PHB occurs in nature not only as the high-molecular-weight microbological storage material (s-PHB, m.w. ca. 10⁶ Dalton) but also as an oligomer of 100–150 units (c-PHB, m.w. around 10⁴ Dalton) supposed to form complexes with various other materials. In her pioneering work, Reusch has shown that c-PHB is present in cell walls of prokaryotic and eukaryotic organisms [10,11], as well as in human blood serum [12]. The proposed function of c-PHB in biological systems called for fundamental synthetic and structural investigations!

We have developed a simple exponential fragment coupling method for preparing linear oligomers of very narrow molecular-weight distribution [13,14] which gave, for instance, a 93-mer I with M₉/M₈ ≤ 1.001 [15], and we found new methods of degrading PHB to oligomer fractions indicative of the dimension of folding in PHB crystals [16,17]. Laser-desorption mass spectroscopy and gel-permeation chromatography were used for molecular-weight determinations, and the synthetic materials served as standards to calibrate these methods [15].

Cyclic oligomers (oligolides) 2 of 3-hydroxybutanoic acid were prepared from the monomer, using macroinitiation methods. Depending on the conditions, different ring sizes were preferred, and pure compounds containing three to ten HB units were isolated [13,14,18]. Especially the smaller oligolides can also be obtained directly from the polymer: under carefully controlled acid-catalyzed conditions, the triolide is prepared from PHB in ca. 50% yield [14,19]. A number of X-ray crystal structures [14,18] reveal the following facts: i) the larger oligolides (≥ 6 HB units) occur in several forms which differ in the folding of the rings (conformation) in the crystals; ii) the folded rings contain structural units from which known [20] and hitherto not detected helical structures of the linear polymer can be modelled [14,21]. A database of bond lengths, bond angles, and dihedral angles for further modelling of polyester structures has become available. The crystal structures of the oligolides and their solid-state NMR spectra have been compared [22]. Finally, enzymatic degradation


